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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/025,335	12/18/2001	Roger Coleman	PF-0198-1 CON	4775

27904 7590 11/19/2003

INCYTE CORPORATION (formerly known as Incyte Genomics, Inc.)
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
KAUFMAN, CLAIRE M	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 11/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

KC

Office Action Summary	Application No.	Applicant(s)	
	10/025,335	COLEMAN ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on th cov r sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-18,28 and 29* is/are pending in the application.

4a) Of the above claim(s) *1,2,11,14-18,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-7,9,10,12 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-7,9-18,28 and 29* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1201* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in the paper filed 9/3/03 is acknowledged. Note that claim 10 was inadvertently left out of Group II (claims 3-7, 9, 10, 12 and 13). The traversal is on the ground(s) that examination of at least Groups I and IV could be made with Group II without an undue burden because the searches for each would overlap. This is not found persuasive because even though searches might overlap, each invention must be thoroughly searched in and of itself, so that multiple searches in the instant case would be burdenson. This is further shown by the different classification of each invention. The broad language in the claims (*e.g.*, 95% identity) further enlarges the search required for each invention. Also, a search for each group is directed to references which would render the invention obvious as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter.

The requirement is still deemed proper and is therefore made FINAL.

As to rejoineder of the methods of Groups V, VI and VII:

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined

claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Specification

The disclosure is objected to because of the following informalities: on page 34, line 19 in the listing of conditions or disease that can be diagnosed with HCOR "remove damaged tissues, and prepare the region...." are not conditions for diagnosis.

Appropriate correction is required.

Claim Objections

Claims 3 and 4 are dependent claims are objected to for depending on non-elected claims.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 3-7, 9,10, 12 and 13 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

It is stated that the present encoding polynucleotide, which has not actually been expressed, encodes a C5a-like receptor named HCOR (p. 3, lines 6-7). It is stated that the instant HCOR (SEQ ID NO:1) is 25% identical to human C5a (p. 11, lines 20-28, and Figure 2).

Gerard et al. (Ann. Rev. Immunol., 12:775-808, 1994, #7 cited by Applicants) discloses that the C5a receptor has sequence homology to other G protein-coupled receptors, such as purinoreceptors (Ibid., Figure 2) and about 34% homology to the formyl peptide receptor (FRP, p. 783, beginning of 4th paragraph). This FRP receptor value is higher than that shown for the instant application's encoded protein and C5a. HCOR also shows about 25% identity with a possible purinergic receptor (6H1 or P2Y5, Webb et al, Biochem. Biophys. Res. Comm., 219:105-110, 1996, #18 cited by Applicants). Sequence homology does not provide a clear answer to specific type of receptor, though it can suggest receptor family relationships. Relationship is particularly difficult to assess when dealing with sequence homologies as low as 25%. The diversity of activities and modes of action are so great for the GPCR family that to say that a protein is a member does not provide a specific or substantial utility (*e.g.*, serotonin receptor compared to rhodopsin photosensitive receptor). Applicants admit that GPCRs mediate diverse functions. Utility of one or multiple species of a class does not necessarily provide utility for all species of the class as a whole.

Further, no ligand has been identified for the encoded HCOR protein. One cannot reasonably assume based on low sequence identity that the ligand for HCOR is C5a, as evidenced by HCOR's homology with other receptors types. Likewise, even though the C5a receptor is involved in inflammation, it is not predictable if HCOR has the same involvement. The use of an orphan receptor to identify ligands is not specific, but is instead a hunting expedition to determine a function or specificity of the receptor. The claims are not restricted generically to the whole family of GPCRs but to particular encoded sequences with unknown functional properties. With regard to use as a diagnostic or therapeutic, if one does not know the specific associated disease or function of the protein, one cannot use the protein therapeutically or diagnostically. There is a list of diverse diseases provided on page 34, lines 12-19, for which

it is said that HCOR may be used for diagnosis, but without knowing which disease is more likely than not to be associated with HCOR and what—at least generally (increased *vs.* decreased levels)—that association is, the claimed invention cannot be used diagnostically.

Page 37 of the specification discusses means of using the encoded polypeptide or fragment thereof or encoding nucleic acid for screening, such as gene mapping and drug screening. Again, if there is no association of the nucleic acid or encoded polypeptide with a disease or condition, these uses are not substantial.

Included in the claimed products are those polynucleotides that do not encode the disclosed HCOR sequence of SEQ ID NO:1 (*e.g.*, claim 12(b)). For these products, there is no specific function recited for the non-identical encoded polypeptides or the polynucleotides that encodes polypeptides not identical to SEQ ID NO:1. Further, there is no limitation on what is the biological activity of a "biologically active fragment" is (*e.g.*, claim 1(c) upon which claim 3 depends), so that the activity need have nothing to so with inflammation. If there is no utility for the full-length polynucleotide of SEQ ID NO:2, there is no utility for a fragment thereof. Aside from a distant structural relationship, there is nothing to suggest a specific function or association that leads to a specific and substantial or well established utility.

The instant claims are drawn to a polynucleotide that encodes at least a fragment of a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that HCOR of the instant application was, as of the filing date, useful for diagnosis, prevention and treatment of cancer or inflammation associated disorders listed on page 34 of the specification. Until some actual and specific significance can be attributed to the protein identified in the specification as HCOR, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-7, 9,10, 12 and 13 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. It is unpredictable if the claimed polynucleotide encodes a C5a receptor. The prior art supports this unpredictability when identification is based solely on sequence identity.

Additionally for claim 7, the cell includes a cell in a human or that is intended to be placed in a human as part of gene therapy with expression of the polynucleotide in a human patient/subject (paragraph beginning at the end of page 28). Expression by gene therapy is extremely unpredictable and has no support in the prior art for wide application of the method. There is no showing in the specification that integration into appropriate cells' transcription pathway or translation of a nucleic acid encoding SEQ ID NO:10 would be possible within a cell in an animal. There is insufficient guidance to allow the skilled artisan to practice the method by the manner claimed with a reasonable expectation of success and without undue experimentation.

Claims 3, 6, 7, 9, 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO:2, the sequence of the nucleic acid encoding the HCOR protein having the sequence of SEQ ID NO:1. SEQ ID NO:2 meets the written description and enablement provision of 35 USC § 112, first paragraph. However, the claims are

directed to or encompass sequences that are at least 90% identical to SEQ ID NO:2 and have a *naturally occurring* sequence or that encode a polypeptide comprising a *naturally occurring* sequence at least 90% identical to SEQ ID NO:1, which sequences would include those of species homologues, allelic variants, splice variants, and so forth. None of these non-identical sequences that must also be isolatable from nature meets the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequence referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NO:2 or a polynucleotide encoding SEQ ID NO:1 (for claim 3), but not the full breadth of the claims meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 9 and dependent claims 6, 7 and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3, 9 (as they depend from non-elected claim 1) and 12 are indefinite because it is not clear what is meant by "naturally occurring". This appears to be a product-by-process limitation but it is not clear what distinguishes a "naturally occurring" polypeptide or polynucleotide from one that is not. The metes and bounds of the claim cannot be determined. For example, it is not clear if a polynucleotide produced by PCR but having the same sequence as a polynucleotide isolated from a natural source would be considered to be naturally occurring.

Claims 3 and 9 (as they depend from non-elected claim 1) use the term "biologically active," which is defined in the specification (p. 6, lines 8-9) as follows: "as used herein, refers to a protein having structural, regulatory, or biochemical functions of a naturally occurring molecule." It is unclear what a structural function is. This appears to be contradictory in that structure can dictate function but not be a function in itself. Also, if the function of naturally occurring SEQ ID NO:1 is not known, one cannot know what is included by the definition of the specification. Therefore, the metes and bounds of the claim are not clear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 U.S.C. §120 states that:

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor

or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application. No application shall be entitled to the benefit of an earlier filed application under this section unless an amendment containing the specific reference to the earlier filed application is submitted at such time during the pendency of the application as required by the Director. The Director may consider the failure to submit such an amendment within that time period as a waiver of any benefit under this section. The Director may establish procedures, including the payment of a surcharge, to accept an unintentionally delayed submission of an amendment under this section.

Claims 3, 6, 7 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Gerard et al. (Nature 349:614, 1991, #5 cited by Applicants).

Gerard et al. teach a polynucleotide encoding a polypeptide of C5aR (Fig. 4a). The amino acid sequence VFLVG (amino acids 47-51) is a fragment of SEQ ID NO:1 of the current application. Because the instant specification says on p.25, lines 14-15, that fragments used to induce antibodies to HCOR include those consisting of at least 5 amino acids, the polynucleotide encoding C5aR of Gerard et al. is a polynucleotide encoding a polypeptide comprising an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1.. Also taught is the polynucleotide in a pCDM8 expression vector and a COS-7 host cell containing the vector (legend of Fig. 3). The polypeptide was produced by culturing the host cell and recovering the polypeptide as required for the ligand binding assay (Fig. 3a and 1a).

Claims 3, 4, 6, 7, 9, 10, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobs et al. (US Patent 5,723,315, #1 cited by Applicants).

Jacobs et al. provided a written description of the claimed polynucleotide. Applicant is advised that the instant application can only receive benefit under 35 U.S.C. §120 from an earlier application which meets the requirements of 35 U.S.C. § 112, first paragraph, with respect to the claimed invention. Because the instant application does *not* meet the requirements of 35 U.S.C. § 112, first paragraph, due to lack of utility for the reasons given above and it is a continuation of application of Serial Number 08/791,974, the prior application also does not meet those requirements and, therefore, is unavailable under 35 U.S.C. § 120. For the purpose of this art rejection, the effective filing date is the filing date of the instant application, 12/18/01.

Jacobs et al. teaches a polypeptide consisting of an amino acid sequence (SEQ ID NO: 28) which is 100% identical to the instant SEQ ID NO:1. Also taught is the double stranded

polynucleotide encoding the polypeptide deposited as clone H963_20 in a transfected *E. coli* (col. 13, line 65 – col. 14, line 33). Also taught is operable linked of the polynucleotide to an expression control sequence in a expression vector and a method for recombinant production and subsequent isolation of the encoded protein from a transfected cell (col. 16, lines 37 through col. 17, line 54).

Claims 3, 6, 7, 9, 12 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruben et al. (WO 98/54206).

Ruben et al. provided a written description of the claimed polynucleotide. As discussed above, neither the instant application nor parent 08/791,974 meets the requirements of 35 U.S.C. § 112, first paragraph. Therefore, for the purpose of this art rejection, the effective filing date is the filing date of the instant application, 12/18/01.

Ruben et al. teach the polynucleotide of SEQ ID NO :33, which is 71% identical to SEQ ID NO :2 of the instant application (see attached Sequence Comparison), and includes at least 60 contiguous nucleotides identical to SEQ ID NO:2 and necessarily the corresponding encoded amino acids (*e.g.*, a biologically active or immunogenic fragment of) SEQ ID NO: 1 of the instant application. Also taught is operable linked of the polynucleotide to an expression control sequence in a expression vector and a method for recombinant production and subsequent isolation of the encoded protein from a transfected cell (p.74, line 19, through p. 76, line 20).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (703) 305-5791 (changing to (571)272-0873 on 01/21/04). Dr. Kaufman can generally be reached Monday through Thursday from 8:30AM to 12:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (703) 308-6564 (changing to (571)272-0871 on 01/21/04).

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

November 14, 2003